



UNITED STATES DEPARTMENT OF COMMERCE
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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/065,676 05/21/93 ILLUM

15M1/1220

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L	EPC148
EXAMINER	
KISHORE, G	
ART UNIT	PAPER NUMBER

4

1502
DATE MAILED:

12/20/93

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|---|--|
| 1. <input checked="" type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input checked="" type="checkbox"/> Notice of Draftsman's Patent Drawing Review, PTO-948. |
| 3. <input type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449. | 4. <input type="checkbox"/> Notice of Informal Patent Application, PTO-152. |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/> _____ |

Part II SUMMARY OF ACTION

1. ☒ Claims 1-14 are pending in the application.
Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-14 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☒ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received
☐ been filed in parent application, serial no. 071842/351; filed on 3-24-92.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

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Claims 1-2 and 5-14 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited spheres made of the components recited in claim 3. See M.P.E.P. §§ 706.03(n) and 706.03(z).

Applicant has not adequately taught what others besides those recited in claim 3 possess bioadhesive properties and could be used in practicing this invention.

Claims 3-4, 6 and 8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

"derivatives" in claim 3 is indefinite; specific derivatives should be recited (petrolite corp. USPQ 113, p. 248).

Does applicant means cross-linking by the expression used in claim 6? Heat is known to cross-link collagen for e.g.

The specific compounds in claim 8 are deemed to be included in "surfactant" which is also recited.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-5, 11 and 13 are rejected under 35 U.S.C. § 102(e) as being anticipated by Illum 4,847,091.

Illum discloses the same invention. (Note the abstract; column 1, lines 15-48; examples and claims).

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The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-14 are rejected under 35 U.S.C. § 103 as being unpatentable over Illum 1986.

Illum (1986) discloses albumin starch microspheres which could be used to deliver drugs including peptides and proteins to the nasal mucosa. She further discloses that the microspheres could be modified by cross-linking (note the discussion section on page 207). According to Illum such a system would ensure an increased time of contact between the delivery system and the mucosa by a process of broadhesion with the possibility of additionally releasing the drug from the system in a sustained and controlled manner (note the 3rd paragraph on page 206. The important factors including the particle sizes are also disclosed by Illum (pages 206-207). Pump spray is disclosed on page 208.

Although Illum's teachings do not include the use of penetration enhancers, her disclosure include the knowledge in the art of the use of such enhancers for nasal (mucosal) delivery of proteins (see 3rd paragraph, introduction). The instant invention is deemed to be an obvious extension of Illum. The criticality of the limitation in claim 12 is not readily apparent to the examiner.

Claims 7-12 and 14 are rejected under 35 U.S.C. § 103 as being unpatentable over Illum 4,847,091 or Illum (1986) in view of Hansen et al. or Salzman et al. and Vice Versa.

Illum 4,847,091 does not teach penetration enhancers.

Illum (1986) although teaches the awareness in the art of penetration enhancers, does not use these enhancers in the microspheres.

Hansen et al. disclose that biological response to nasal administration of calcitonin could be increased by inclusion of various surfactants in the formulation (see "conclusions" on page 241). Hanson's et al.'s disclosure does not include the use of microspheres. An artisan could, however, interpret Hanson et al.'s term "formulations" as inclusive of microspheres.

Salzman et al. disclose that intranasal administration of insulin in combination with a non-ionic detergent increases the absorption of insulin (note discussion on page 1081). Salzman et al.'s disclosure, however, does not include microspheres.

To include penetration enhancers such as surfactants taught by Hanson et al. or Salzman et al. in the microspheres of Illum or Suzuki et al. (assuming phospholipids are not penetration enhancers) for nasal delivery for drugs including insulin would have been obvious to one of ordinary skill in the art at the time

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the invention was made since such an inclusion would certainly increase the absorption of drugs by mucosal membrane.

Alternatively, to use the microspheres of starch or similar swellable and broadhesive material as taught by Illum (1986) Illum (4,847,091) in the teachings of Hanson et al. or Salzman et al. would have been obvious to one of ordinary skill in the art since such spheres adhere to the nasal mucosa and allow the drug to be released in a sustained manner.

L & V are cited of interest.

Any inquiry concerning this communication should be directed to G. S. Kishore, Ph.D. at telephone number (703) 308-2440.

G. S. Kishore
GOLLAMUDI KISHORE
PATENT EXAMINER
GROUP 1500

G. S. Kishore, Ph.D.:cb
December 08, 1993